

# Strategies for the Prevention of Development of Pesticide Resistance in the UK—Lessons for and from the Use of Herbicides, Fungicides and Insecticides\*

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**Abstract:** Since the 1950s, pesticide resistance has been identified in many species. This paper considers the role of resistance action groups and notes that they were all formed in response to resistance problems occurring. Data now exist on the strategies which are most effective and the paper aims to bring together information from the fields of weeds, pests and diseases. Pesticide mixtures, sequences or rotations have been demonstrated as having a clear role in resistance management strategies. Resistance management would be improved if there was agreement on uniform test methodology and interpretation of results. The industry must work together to agree what constitutes an anti-resistance strategy, whether this is for prevention or cure, and to ensure that this is then included within regulatory frameworks. Future developments such as patch treatment, biotechnology and biocontrol are discussed. It is concluded that, to date, there has been little discussion between specialists in the field of resistance to herbicides, fungicides or insecticides and it is clear there are significant advantages to be had from more interaction.

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## 1 INTRODUCTION

Use of pesticides has revolutionised modern agriculture and enabled the increased level of food production required. In early years this led to few problems, but, increasingly, weeds, pests and diseases have developed resistance to several of the pesticides used in agriculture today. The first report of insecticide resistance was made in 1914.<sup>1</sup>

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The incidence of resistance to insecticides increased rapidly after 1950 and resistance to fungicides after 1960. By the late 1980s there were over 500 species of pest and over 150 fungal pathogens which showed resistance to pesticides.<sup>2</sup> The development of weeds resistant to herbicides is more recent, despite the widespread use of selective herbicides for over 40 years. The first report,<sup>3</sup> of triazine resistance in *Senecio vulgaris* L., was in 1968. Since then 113 resistant biotypes have been reported,<sup>4</sup> still fewer than with fungicides and insecticides. Pesticide resistance is now considered important in the management of many weeds, pests and diseases in the UK. However, there is very little economic or objective information on the relative importance and areas affected by resistance to weeds, pests or diseases. The major weed species which have developed resistance to

herbicides in the UK are *Alopecurus myosuroides* Huds., *Avena* spp. and *Lolium multiflorum* Lam. In addition, several broad-leaved weeds have evolved resistance to triazine herbicides. *Myzus persicae* Sulz is the most important insect pest of UK field crops which has developed resistance to insecticides. The most important UK pathogens in which resistance has developed are *Pseudocercospora herpotrichoides* Deighton in cereals, *Erysiphe graminis* DC f.sp. *hordei* Marchal in barley and *Phytophthora infestans* (Mont.) deBary in potatoes.

The manufacturers' response to resistance problems was to form resistance action committees such as IRAC (Insecticide Resistance Action Committee; founded in 1984) and FRAC (Fungicide Resistance Action Committee; founded in 1981) to co-ordinate efforts by manufacturers of fungicides to introduce effective anti-resistance strategies. HRAC (Herbicide Resistance Action Committee) was founded in 1989. All report to GCPF (Global Crop Protection Federation, formerly GIFAP), have a worldwide remit and consist entirely of representation from industry with no independent or government representation. In the UK, resistance action groups were formed to have representation from a wide range of interests, including independent organisations and the agrochemical industry. The first of these was WRAG (Weed Resistance Action Group) which was formed in 1989, just pre-dating the HRAC. Since then FRAG (Fungicide Resistance Action Group) was formed in 1995 and IRAG (Insecticide Resistance Action Group) is to be formed in 1997.

During this time, little opportunity has been taken by experts in the different disciplines of pesticide resistance to discuss the issues relating to weeds, pests and diseases. This paper aims to bring together this expertise, identify similarities and differences between approaches and to draw conclusions about the management strategies to adopt and make recommendations for future priorities. It will consider the way in which the strategies are formulated and promoted, as well as their content.

## 2 INSECTICIDES

Since 1914 insecticide resistance has been an increasingly important factor in insect control. By 1984, 1797 cases of resistance in arthropods had been reported worldwide and by 1991 resistance to at least one insecticide had been recorded in 504 species.<sup>5</sup> By 1984, at least 17 insect species were reported to be resistant to all major classes of insecticides.<sup>6</sup> One species, *M. persicae*, was identified as being resistant to more insecticides than any other species. By 1991, resistance to 71 synthetic insecticides had been detected in various populations of *M. persicae* worldwide. The next most

resistant insect species were identified as *Leptinotarsa decemlineata* Say and *Plutella xylostella*.<sup>7</sup> It might seem from the above that resistance to insecticides is a major problem but, in effect, it is not very significant for most UK arable crop growers.

Resistance to insecticides was defined by Georgiou & Mellon.<sup>8</sup> An invertebrate population is considered resistant if its response in detection tests drops below its normal response. For most growers and their advisers a population would be considered resistant if the degree of control given by the pesticide was less than expected, with no other factors, such as application problems, extremes of temperature, etc. implicated. The definition of Georgiou & Mellon would not necessarily be accepted by plant pathologists and others, as the use of terminology appears to differ between (and possibly within) the various disciplines.

Resistance to insecticides is predominantly the result of an altered target site or an enhanced ability to metabolise toxins.<sup>9</sup> Until growers know that the populations they are trying to control contain resistant variants, or are likely to, it will be assumed that the population is susceptible and the choice of insecticide will be made according to factors such as efficacy, price, crop type and growth stage, personal preference and advice. Any strategy to prevent the development of resistance at this stage is likely to be considered by the manufacturer and/or regulatory authorities such as the Pesticide Safety Directorate (PSD) rather than developed by the grower. Although there has been much discussion over the years about the best strategy for using insecticides where evolution of resistance was likely, there was no agreement and subsequently no promulgated strategy for delaying the occurrence of resistance.

Once growers know from past experience that a pest population is likely not to be controlled by an insecticide or group of insecticides, they will choose a product that is more likely to work, based on experience, advice and information. At this stage the likely advice will be not to overuse an effective chemical, an injunction reinforced on the label. It is currently unusual to have a restriction on the number of applications of chemicals from an effective group. Other restrictions are usually of the form that the product is unlikely to give satisfactory control of resistant strains. More specific advice is rare and associated with the newer insecticides. For the use of imidacloprid (a relatively new insecticide to the UK) against aphids on hops, the instruction not to treat all the crop in any one year with this product is given with the stated aim of minimising the likelihood of resistance developing. For imidacloprid used in composts, there is a stipulation that pesticides of different types or other control measures should be alternated in a planned programme to delay the development of resistance, rather than relying totally on one pesticide.

So far, the development of resistance in a UK arable insect species has been offset by the introduction of new,

effective insecticides. Insecticide resistance has generally been a bigger problem for protected crops growers in the UK, where pests such as *Aphis gossypii* Glov., *Bemisia tabaci* Genn., *Frankliniella occidentalis* Perg., *M. Persicae*, *Tetranychus urticae* Koch and *Trialeurodes vaporariorum* Westw. have shown resistance to most, if not all, pesticides for several years. Such wide-scale resistance was one reason for the development of biological control of pests on protected crops and this approach must be a way forward on arable crops too. Increasingly, the development of resistant crops includes the use of transgenic resistance from other species and/or the gene for the production of the toxin in *Bacillus thuringiensis* Berliner (Bt). However, work by Tabashnik *et al.*<sup>10</sup> has indicated that Bt-modified plants may not be effective for long against *P. xylostella*, as resistance to strains of Bt is relatively common in populations of the moth. Such abilities also need to be taken into account in formulating control strategies.

### 3 FUNGICIDES

There are clear examples where the use of fungicide mixtures can prevent the development of fungicide resistance.<sup>11</sup> This policy of the use of fungicide mixtures must be implemented before resistance is confirmed. Introducing mixtures once resistance to one of the partners is widespread is rarely effective. This is particularly important in situations where the resistant forms of the population are 'fit' i.e. they can compete and survive in the 'wild-type' population (as was the case with many benzimidazole-resistant strains). Clear examples of resistance development due to the use of a single-site mode-of-action product did not deter the agrochemical community from repeating the mistake several more times during the 1980s and 1990s. The introduction of phenylamide fungicides applied alone for the control of *P. infestans* in Ireland and Holland led to resistance in field crops in 1980, and to the withdrawal of the products from these countries in 1981. In the UK, where phenylamide fungicides for *P. infestans* control were available only in a formulated mixture, resistance development was very much slower and field resistance problems were rare.<sup>12</sup> This type of fungicide resistance, where field resistance means virtual total loss of control, forced manufacturers to seriously consider the use of mixtures as a means of protecting their products in the marketplace.

Despite earlier experiences, the development of resistance to the DMI (demethylation inhibitor) group of fungicides (e.g. triadimefon) in wheat and barley mildew in the 1980s had not been predicted. In fact, the belief was that, because resistant strains in the laboratory were less fit than wild-type strains, the likelihood of field

resistance developing was very small.<sup>13</sup> It was found that, whereas the resistance to phenylamides and benzimidazoles was due to a single gene mutation and caused a major change in sensitivity, resistance to the DMI fungicides was multigenic, resulting in small changes in sensitivity.<sup>14</sup> Because of the small changes in sensitivity to such fungicides, the loss of activity was not complete and in many cases the decreased performance could be overcome by using higher rates, shortening the intervals between use or by using more effective products from the same fungicide group. This led to considerable debate in the industry about whether field resistance actually existed, allowed users to continue to get good control by using the better products from this group, but also damped down the industry's concerns about fungicide resistance in general. Had resistance to the DMI fungicides happened in the same way as to the benzimidazoles, then the industry would have reacted very differently and perhaps developed serious anti-resistance strategies. Instead, fungicide resistance now fuels considerable academic debate but has little impact on most growers. The industry pays lip-service to anti-resistance strategies, the regulatory authorities require 'a management strategy designed to minimise the likelihood of resistance . . .' to be provided<sup>15</sup> but, in practice, single-site fungicides are still most commonly sold and used alone. Until 1997 cereal growers in the UK had little choice in terms of fungicide groups from which to devise a mixture or alternation policy. However, 1997 saw the introduction of the strobilurin analogues, a group of highly active compounds which are perfect partners to the DMI fungicides which have dominated the market until recently. Despite the availability of several new groups of fungicides as ideal partners in fungicide mixtures, most manufacturers have introduced single active ingredient products. This was despite the experiences of the 1970s and 80s which clearly demonstrated that, if resistance is to be prevented, fungicide mixtures should be used before any changes in sensitivity are detected. A notable exception to this is the sale of fungicides for *P. infestans* control where mixtures predominate. With the sale of two- and three-way fungicide mixtures being commonplace, perhaps the manufacturers learned a valuable lesson during the 1980s when phenylamide resistance almost destroyed a marketing opportunity. Although FRAC could claim credit for this policy, it was in response to a very serious threat of loss of sales to most of the manufacturers of phenylamide products. Where they all had a common goal, as with phenylamide resistance, the committee worked well. However, in the cereal crop, where sales of single products are high and increasingly active products are being marketed, the threat of sensitivity shifts in pathogen populations seems not to warrant any concerted effort to market mixtures. Where fungicide mixtures are sold, it is invariably due to commercial reasons and not as an anti-resistance strategy.

#### 4 HERBICIDES

Those involved within the herbicide sector have tried to work together from the earliest opportunity to form a consensus view on appropriate strategies. This was reflected in the desire to form the Weed Resistance Action Group (WRAG) at the outset. In 1991, WRAG produced its first guidelines for the prevention and control of herbicide-resistant *A. myosuroides*. These were updated and given wider circulation in 1993.<sup>16</sup> These guidelines placed great emphasis on cultural control measures and identified three situations linked to the degree and risk of resistance problems. These situations, in increasing order of severity, were:

1. fields where consistently good *A. myosuroides* control had been achieved, or where reduced herbicide activity was known to be due to factors other than resistance;
2. fields where herbicide performance had been inadequate (especially where performance had tended to decline over a period of years), and the reasons for this reduced activity had not been identified;
3. fields where herbicide-resistant *A. myosuroides* had been positively identified by testing plants or seed samples. This included nearby fields where a similar husbandry system was practised.

Within these situations, the adoption of cultural measures was stressed throughout, as was the adoption of mixtures and rotations of herbicides from different herbicide groups. The cultural control measures recommended included factors such as ploughing, crop rotation, spring cropping, delayed autumn sowing, stubble hygiene, competitive crops and in-crop cultivations. Since publication of the guidelines, 'set-aside' has correctly assumed a greater importance as a cultural strategy. In recent years, attention has also turned to reminding farmers and others of measures to prevent seed return and spread. However, it is important to question how much of this cultural information has been put across to the farmer and whether it was done at the right time. The strategies for herbicide use were: (1) to avoid the use of the aryloxyphenoxypropionates ('fops') and cyclohexanediones ('dims') as the sole or main means of control in consecutive crops. This reflects the risk of rapid development of severe resistance to these herbicides; (2) to consider the use of sequences of herbicides. In winter cereals these would commence with tri-allate or trifluralin, and be followed by isoproturon (a herbicide to which development of resistance is much slower). Within the break crops, such as oilseed rape, a wider range of products is available, although the 'fop' and 'dim' herbicides are often the most effective; (3) other recommendations included advice not to apply more than the maximum recommended dose of any single active ingredient to any single crop, and that

timing of herbicide applications is even more critical than in normal situations, so parameters such as recommended dose, water volume and spray quality should be carefully adhered to.

This message has been promoted widely in the farming press and received Home-Grown Cereals Authority (HGCA) levy funding for publication of these guidelines. The activities of WRAG have to date concentrated on herbicide resistance in *A. myosuroides* although increasing attention will be paid to *Avena* spp. Although not universally accepted in every detail these strategies have been widely recognised. A voluntary statement referring to the Guidelines has also been included on some herbicide labels.

#### 5 ISSUES

By looking at the way in which issues have been approached in different disciplines it is possible to draw together conclusions aimed at improving the way in which the issue of pesticide resistance is handled within the agricultural industry.

##### 5.1 Reactive or proactive

To date, the formation of the Resistance Actions Committees (RACs) and Resistance Action Groups (RAGs) in the UK has been as a result of resistance problems being recognised by the agrochemical industry. Equally, registration authorities and farmers have only reacted once there is a problem. Throughout the world, and especially in Australia where problems with herbicide resistance are widespread,<sup>17</sup> farmers have only reacted once resistance is confirmed on their farm. Resistance problems are continually increasing and there is now some shift towards preventing resistance development rather than reacting to it. For instance, proposed EU registration requires that 'where available, information on possible occurrence of the development of resistance or cross-resistance must be provided.'<sup>18,19</sup> To be effective, strategies which prevent resistance need to be initiated when a new pesticide is introduced and these may increase product life. To date, RACs and RAGs have been effective in slowing development once resistance has been observed. They should, perhaps, play a more effective role in preventing it in the first place.

##### 5.2 Mixtures and sequences

There is good information on the short-term benefits of mixtures or sequences in resistance management, but less information relating to their robustness in the long-term. However, it is important that mixtures and sequences are effective in assisting management strategies. Attempts to describe mixtures efficacious in pre-

venting herbicide resistance have been made.<sup>20</sup> They state that components should ideally have the following traits: (a) control the same spectrum of weeds; (b) have the same persistence; (c) have a different target site; (d) be degraded in a different manner and (e) preferably exert negative cross-resistance. So, to be useful in resistance management, the mixture needs components with different modes of action and with both components effective. As soon as one component becomes less dominant, the risk of resistance developing is increased. These principles have not been well adopted or applied, both because no herbicide mixture fulfills all these criteria and for commercial reasons.

Historically, it is clear that fungicide mixtures, if marketed as the sole method of obtaining active ingredients, can prevent or at least delay the onset of fungicide resistance. This simple fact has not been used in the development of anti-resistance strategies for most arable crops. The major exception is fungicides for controlling *P. infestans*, which are now marketed almost exclusively as mixtures. Why is this?—is it purely for the commercial reason of prolonging the life of existing products in a market where all major players had the same problem, or is it genuine resistance management?

There are major marketing reasons why mixtures or sequences have not been widely adopted from launch of products. To be more proactive and maintain product life, selling in mixtures from launch would be of benefit. Pressures in the other direction include the desire from pesticide distributors to have the flexibility to sell 'customised' tank-mixtures of their own and hence to have access to single active ingredients.

### 5.3 Dose and selection pressure

There has been considerable debate on the risk of resistance associated with dose of herbicide applied. Focusing on dose has proved to be a distraction where concentration on selection pressure is more relevant. It is easy to construct arguments why both high and low dose influence the development of resistance. It will help promotion of suitable strategies if prominence is given to the role of selection pressure and debate about dose is curtailed.

### 5.4 The responsibility for resistance management

Through the requirements of the pesticide registration system, agrochemical manufacturers have a responsibility for resistance management. This is very important, especially for fungicides and insecticides, because the actions of an individual farmer are influenced by the attitude of neighbours. Even if the farmer adopts a perfect anti-resistance management strategy himself, spread of pests and diseases in the locality will depend on the strategies adopted by others. This is less

important with weeds, because the actions of an individual farmer determine to a much greater extent the problem faced. There is minimal spread to other farms in the locality, although gene flow in pollen is possible.

This belief by farmers that resistance is not their problem and that pesticide companies will come up with an answer has too often been proven correct. To date, pesticide manufacturers have come up with alternative products and kept ahead of resistance development, or resorted to older products which have multi-site activity and are less affected by resistance. Without legislative pressure there is little likelihood of the agrochemical industry adopting robust anti-resistance strategies, such as selling products only in mixtures.

### 5.5 Testing methodology and interpretation

There is clear scope for improved standards of test methodology and interpretation of results. In many areas of resistance there is no agreement on the appropriate test, comparison between methods or agreed interpretation of test results. This severely hinders the adoption of appropriate strategies because of the confusion of levels of resistance and subsequent need for action. The only real attempt to standardise has been with *A. myosuroides* where test methodology has been published, along with interpretation of results based on standard reference populations.<sup>21</sup> This is now being taken further into a European 'ring test' among 16 organisations carrying out testing on a range of standard populations. However, it is disappointing that the interpretation is not adopted universally by all organisations carrying out tests. Resistance management would be improved if there were greater agreement on correct test methodology and interpretation of results. The use of the term 'resistant' is not universally agreed either. Some refer to 'tolerance' and others 'insensitivity'. Others refer to a population as being resistant if the pesticide fails to give control due to inactivity, where no control was ever claimed on pesticide labels. In practical terms, to a farmer a weed, pest or disease becomes resistant to a pesticide if the full dose of application, correctly applied, no longer gives acceptable control—a definition that the industry needs to concentrate on to improve resistance management.

### 5.6 Development of strategies and their promotion

There is no industry-wide agreement on what constitutes a strategy to combat resistance. Pesticide labels have bland statements which purport to give advice on anti-resistance measures but which the user has little or no incentive to follow—even if the advice is sound. The regulatory authorities share the blame, as they claim to demand anti-resistance policy statements on labels, but

'... do not apply more than three applications in one season' does not qualify as a realistic anti-resistance strategy in a cereal crop. Statements of advice to 'alternate the product with other products with different modes of action' are little better, being often impractical, and even impossible. It is important that the industry works together to agree what constitutes an anti-resistance strategy, that this is for prevention rather than cure (which has been the case in the past) and that this is then included within product development, regulatory framework, RAG and RAC guidelines and on pesticide labels.

Attempts at an agreed strategy are to be encouraged. Examples exist for *A. myosuroides*<sup>16,22</sup> published under the banner of WRAG and fungicide resistance<sup>23</sup> published by FRAG. The industry will benefit from clear agreed statements of strategy which minimise confusion. However, it is important that such strategies do not lack substance because of the need to reach compromise and acceptability to commercial interests. The way in which the strategies are promoted to the industry is important. There is no one correct way of doing so, but it is important to remember that the messages are often complex and must be conveyed with clarity. Use of a range of media to attract various recipients is necessary. Strategies will contain the best available information, but it is recognised that, in many areas, more information is required to be effective. A most robust strategy would be the marketing only of mixtures.

### 5.7 The future

Future developments are held out by some as offering improved resistance management. One such development is patch spraying. Modern technology allows sprayers to apply treatments to small patches within fields. This could offer some reduction in selection pressure by leaving susceptible plants in unsprayed areas. However, within the patch the selection pressure will be unchanged from previous management. Opportunities for controlling resistance development may exist but need to be carefully researched.

Another development is from biotechnology and the introduction of herbicide-resistant crops. The principle of plant breeding for improved pest and disease resistance is well established. Biotechnology is an extension of this opportunity. Clearly, improved natural resistance to pests and diseases will reduce pressure on pesticides and assist in anti-resistance strategies. The introduction of herbicide-resistant plant genes is a different matter. There are both benefits and risks from the introduction of this technology. This will introduce populations of plants which are known to have herbicide resistance, something we have been striving to avoid happening in weed species. Unfortunately, volunteer crops are them-

selves now a major weed problem which farmers have to face. The addition of herbicide-resistant volunteers will add to this problem. On the positive side, the herbicides to which resistance has been introduced (such as glyphosate and glufosinate) are not used selectively in arable crop production and are considered to pose a low risk for selection of resistant biotypes. One benefit is to allow the control of herbicide-resistant populations of weeds by using herbicides of different activity. The introduction of such genes needs careful appraisal, which is beyond the scope of this paper.

Advances in biocontrol will also aid resistance management strategies. Already biocontrol has been introduced to combat pest resistance, particularly in glasshouse conditions. Significant opportunities exist in pest and disease control from biocontrol but at present opportunities are limited for weed control (other than the cultural control measures outlined earlier).

## 6 CONCLUSIONS

Substantial data now exist on the strategies which are most effective. Mixtures, particularly of fungicides, have been demonstrated as having a clear role in resistance management strategies. Despite this, single active ingredients are introduced and subsequent resistance development has occurred.

Several organisations within the industry have a role in resistance management. An industry-wide attitude is essential for fungicides and insecticides where pests and diseases can be spread irrespective of an individual farmer's resistance management strategy. By comparison, this is less important for weeds, where spread from one field to another is within the farmer's direct control.

There is clear scope for improved standards of test methodology and interpretation of results. The current situation hinders the adoption of appropriate strategies because of the confusion of levels of resistance and subsequent need for action. Resistance management would be improved if there were agreement on uniform test methodology and interpretation of results.

There is no agreement on what constitutes a strategy to combat resistance. It is important that the industry works together to agree what constitutes an anti-resistance strategy, that this is for prevention rather than cure and that this is then included within regulatory frameworks.

So far there has been little interaction between specialists in herbicide, fungicide or insecticide resistance. Writing this paper has brought together experts from these fields and there are likely to be significant advantages to be had from more dialogue. Lessons could even be learnt from other areas where resistance is important, such as pharmaceuticals. In some sectors in the UK, notably herbicides, there is already good

exchange of information and collaboration between researchers, manufacturers, advisers and regulators through collaborative research, WRAG and at other events. In other sectors this is less well advanced. Progress to improve strategies for resistance management needs to be collaborative.

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